

Applicant: Michael J. Heller et al.
U.S. Serial No.: 09/358,788
Filed: July 22, 1999
Page 7 of 11: Amendment In Response To October 18, 2011 Final Office
Action As A Submission Accompanying A Request For Continued
Examination Under 37 C.F.R. §1.114

REMARKS

Claims 49, 57, 58 and 79-82 are pending in the subject application, and claims 1-48, 50-56 and 59-78 were canceled previously. By this Amendment, claims 49, 57 and 82 have been amended to clarify the claimed subject matter.

Support for the amendments to claims 49 and 82 may be found in the specification, *inter alia*, at page 17, lines 5-6; page 42, lines 9-22; page 43, lines 16-19; page 52, lines 22-26; and page 53, lines 5-9.

Accordingly, applicants respectfully request that this Amendment be entered. Upon entry of this Amendment, claims 49, 57, 58 and 79-82 remain pending in the subject application, with claims 49 and 82 being in independent form.

Non-Statutory Obviousness-Type Double Patenting Rejections

In the October 18, 2011 Office Action, the Examiner rejected the pending claims on the grounds of non-statutory obviousness-type double patenting as follows:

(a) pending claims 49, 57, 58 and 79-82 were rejected over claims 1-46 of U.S. Patent No. 6,017,696 in view of Cozzette et al. (U.S. Patent No. 5,063,081) and Hollis et al. (U.S. Patent No. 5,846,708, filed 23 April 1992);

(b) pending claims 49, 57, 58 and 79-82 were rejected over claims 1-46 of U.S. Patent No. 6,048,690 in view of Cozzette and Hollis;

(c) pending claims 49, 57, 58 and 79-82 were rejected over claims 1-37 of U.S. Patent No. 5,849,486 in view of Cozzette and Hollis;
and

(d) pending claims 49, 57, 58 and 79-81 were rejected over claims 1-8 of U.S. Patent No. 7,582,421 in view of Hollis.

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The Examiner alleged that the pending claims are not patentably distinct from the claims of the cited art because each set of claims are allegedly drawn to methods for analyzing a nucleic acid sample by hybridization on electronically addressable microlocations wherein hybridization stringency is electronically controlled to allegedly remove non-specifically hybridized targets. Regarding the double patenting rejection over U.S. Patent No. 6,048,690 in view of Cozzette and Hollis, the Examiner alleged that the claim sets merely differ in that that pending claims define the structure of the electronic stringency control device, e.g., microlocations comprising permeation and attachment layers, while the patent is silent regarding the structure. The Examiner purports that Cozzette teaches the structure of the electronic device allegedly including a permselective layer that allegedly acts as an adhesion promoter for the attachment layer thereby facilitating biomolecule immobilization. The Examiner alleged that it would have been obvious for one of ordinary skill in the art to apply the permselective and attachment layers of Cozzette to the patent electrodes.

Applicants' Reply:

Double Patenting Over U.S. Patent No. 6,048,690

In response to the double patenting rejection over U.S. Patent No. 6,048,690 in view of Cozzette and Hollis, applicants note that claims 49 and 82 have been amended to recite "a continuous and constant electric field". Applicants respectfully submit that the claims of U.S. Patent No. 6,048,690 taken with the cited art do **NOT** disclose or suggest subjecting individually selected microlocations to a continuous and constant electric field which moves unhybridized and partially hybridized sample oligonucleotide sequences away from one or more anchor, following the hybridization step.

An important aspect of the present application is use of a continuous and constant reverse current to completely denature the mismatched strands after hybridization and move the partially

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hybridized and unhybridized sequences away as shown in Figures 2 and 3 and Example 9. According to the present application, detection of the hybridization products can be carried out by various methods, such as further hybridization to a reported probe (page 33, lines 13-15), using a fluorescent or DNA-binding dye (page 35, lines 2-16), etc.

The '690 patent describes methods that take advantage of a fluorescent perturbation phenomenon by monitoring emitted fluorescence after applying a varying electrophoretic force to a hybridization product. (See, column 6, lines 5-9 and claim 1 of the '690 patent). The varying electrophoretic force applied to the hybridization product is pulsed as shown in the Examples (See, column 19, lines 25-32 and column 20, lines 21-24 of the '690 patent). The varying and pulsed electrophoretic force causes the mismatched hybridization site to partially denature and renature relative to the matched hybridization site, (See, column 10, column 15, and Figures 7A-B) thus producing a oscillating fluorescent signal for the mismatched hybridization site while the signal for the matched hybridization site is unchanged as shown in Figures 3C and 4C. According to the methods of the '690 patent, varying or pulsing of the electric field is necessary for observing the fluorescent perturbation effect and thus distinguishing a match from a mismatch.

Applicants respectfully submit that one of ordinary skill in the art would not be motivated to replace the varying or pulsed electric field which is a necessary aspect of the '690 patent with a continuous and constant electric field. Moreover, Cozzette and Hollis fail to disclose use of a continuous and constant electric field.

Accordingly, applicants respectfully submit that the claims of the '690 patent in view of Cozzette and Hollis simply does **NOT** render unpatentable the aforementioned aspects of claims 49 and 82.

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In view of the proceeding remarks and the amendments to the claims,
applicants request that the Examiner reconsider and withdraw her
rejection.

Double Patenting Over U.S. Patent No. 5,849,486

In response to the double patenting rejection over U.S. Patent No.
5,849,486 in view of Cozzette and Hollis, applicants note that the
claims of the '486 patent are directed to methods for analysis of
hybridization based on electronic perturbation of fluorescence and
recites use of varying electric force.

Accordingly, the arguments recited above as applied to the '690
patent apply equally to the '486 patent.

Applicants respectfully submit that the claims of the '486 patent in
view of Cozzette and Hollis simply do **NOT** render unpatentable the
aforementioned aspects of claims 49 and 82.

In view of the proceeding remarks and the amendments to the claims,
applicants request that the Examiner reconsider and withdraw her
rejection.

Double Patenting Over U.S. Patent Nos. 6,017,696 and 7,581,421

In response to the double patenting rejections over U.S. Patent Nos.
6,017,696 and 7,581,421, applicants will consider filing a Terminal
Disclaimer as soon as claims have been indicated to be otherwise
allowable.

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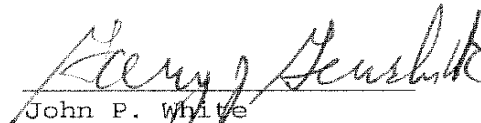
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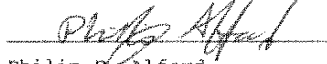
Applicants earnestly solicit allowance of this application. If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the \$75.00 fee for a one-month extension of time and \$465.00 for a Request for Continued Examination, is deemed necessary in connection with the filing of this Amendment. Accordingly, authorization is hereby given to charge \$540.00 to Deposit Account No. 03-3125. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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